Application No.: 10/567,486

Filing Date: February 6, 2006

AMENDMENTS TO THE CLAIMS

- (Previously presented) A method for assessing in vitro the predisposition of a subject to develop cardiovascular pathologies, comprising identifying the nucleotide corresponding to position 436 of seq IDN1 (COX-2 gene PROMOTER) on a sample of genomic DNA of said subject.
- (Previously presented) The method according to claim 1, where the genomic DNA is extracted from cells of such subject, derived from blood samples, saliva, biopsies, urine, human tissue
- (Previously presented) The method according to claim 2, where said cardiovascular pathologies are caused by or associated with rupture of an atherosclerotic plaque.
- 4. (Previously presented) The method according to Claim 1, wherein said cardiovascular pathologies are coronaropathies, pathologies of carotid arteries, myocardial infarction, angina pectoris, acute coronary syndromes, myocardial revascularization by means of coronary by-pass or angioplasty, stroke, transient ischemic attack (TIA), peripheral arteriopathy, trombophylic syndromes.
- 5. **(Previously presented)** The method according to claim 4, wherein said identification is carried out by one of the following techniques: sequencing, endonuclease digestion with restriction enzymes, selective hybridization with oligonucleotides specific for polymorphism at position -765 of the human COX-2 gene promoter, single strand conformational polymorphism (SSCP), DGGE, Fluorescence assisted mismatch analysis (FAMA), heteroduplex analysis, Real Time PCR.
- (Previously presented) The method according to claim 5, wherein said identification is carried out by endonuclease digestion with restriction enzymes.
- 7. **(Previously presented)** The method according to claim 6, comprising the following steps:
 - extracting genomic DNA from a biological sample of the subject,
 - amplifying by means of Polymerase Chain Reaction with oligonucleotides or primers suitable for amplification of a DNA fragment comprising position -765,
 - enzymatically digesting such amplified fragment with a restriction enzyme selected from: Fau I and Aci I

Application No.: 10/567,486 Filing Date: February 6, 2006

> electrophoretically separating the restriction mixture comprising the restriction fragments or of the undigested amplified fragment, or of both,

- analyzing the restriction profile generated after visualization of DNA.
- 8. **(Previously presented)** The method according to claim 7, wherein said amplifying is carried out with oligonucleotides having sequences at least partially identical to sequences ID NO 3 and ID NO 4 and the amplified fragment is digested with the restriction enzyme Fau I.
- 9. **(Previously presented)** The method according to claim 8, wherein said amplifying is carried out with oligonucleotides having sequence SEO. ID NO 3 and 4.
- 10. (Previously presented) The method according to claim 1, wherein the presence of a cytosine (C) at position 436 of SEQ ID NO: 1, in at least one DNA allele of such subject, indicates a lower risk to predisposition to cardiovascular diseases than the risk associated to the presence of a guanosine (G) in position 436 on both alleles.
 - 11. (Withdrawn) A kit for carrying out the method according to claim 1.
- 12. (Withdrawn) The kit according to claim 11, comprising at least one of the following oligonucleotides: an oligonucleotide comprising at least 10 consecutive nucleotides of seq ID NO 3, an oligonucleotide comprising at least consecutive nucleotides of seq ID NO 4 and optionally one restriction enzyme selected from: Fau I and Aci I.
- 13. (Withdrawn) The kit according to claim 12, comprising the oligonucleotide with sequence ID NO 3 and the oligonucleotide with sequence ID NO 4, the Fau I restriction enzyme and optionally one molecular weight DNA standard.
- 14. (Previously presented) A prognostic method for a cardiovascular pathology selected from the group consisting of: coronaropathies, pathologies of carotid arteries, myocardial infarction, angina pectoris, acute coronary syndromes, myocardial revascularization by means of coronary by-pass or angioplasty, stroke, transient ischemic attack (TIA), peripheral arteriopathy, and trombophilic syndromes, comprising genotyping of nucleotide at position 436 of SEQ ID NO: 1 (COX-2 gene promotor).
- (Previously presented) A method of assessing the sensitivity to therapy with non steroidal anti-inflammatory drugs (NSAIDs) comprising genotyping of nucleotide at position 436 of SEQ ID NO: 1 (COX-2 gene promotor.

Application No.: 10/567,486

Filing Date: February 6, 2006

16. (Withdrawn) The kit for carrying out the method according to claim 10.

- 17. (Previously presented) The method according to claim 16 wherein the presence of a cytosine (C) at position 436 of SEQ ID NO: 1, in at least one DNA allele of such subject, indicates a lower sensitivity to therapy with non steroidal anti-inflammatory drugs (NSAIDs) than the presence of a guanosine (G) in position 436 on both alleles.
- 18. (Withdrawn) A kit for assessing the sensitivity to therapy with non steroidal anti-inflammatory drugs (NSAIDs) comprising genotyping a nucleotide at position 436 of SEQ ID NO: 1 (COX-2 gene promotor) with suitable oligonucleotides.
- (Withdrawn) A kit according to claim 18 comprising the oligonucleotides having SEQ ID NO: 3 and SEQ ID NO: 4.